Remarks

The Office Action mailed January 29, 2003 has been received and reviewed. Claims 1-19, 22, 23, and 25-28 having been cancelled, claims 20, 21, 24 and 29-31 having been amended, and claims 32-67 having been added, the pending claims under examination are claims 20, 21, 24 and 29-67. Reconsideration and withdrawal of the rejections are respectfully requested

Support for claim amendments is found in the original claims and throughout the specification. For example, support for amended claim 21 is in the specification on page 14, line 27 through page 15, line 1. Support for new claims 32, 42, 52, and 60 is found in original claim 21. Support for new claims 33, 43, 53, and 61 is found on p. 10, lines 27-28 of the specification. Support for new claims 34, 36, 40, 44, 46, 50, 54, 56, 58, 62, and 64 is found on p. 16, lines 28 to p. 17, line 2 of the specification. Support for new claims 35, 37, 41, 45, 47, 51, 55, 57, 59, 63, and 65 is found on p. 18, line 25 to p. 19, line 1 of the specification. Support for new claims 38, 48, and 66 is found on p. 11, line 23-24 and p. 12, lines 12-13 of the specification. Support for new claims 39, 49, and 67 is found on p. 12, lines 13-16 of the specification.

Objection to the Drawings

The Examiner objected to the drawings, for the reasons set forth in the PTO-948 dated January 24, 2003. Formal drawings are enclosed herewith. Withdrawal of this objection to the drawings is respectfully requested.

The 35 U.S.C. §112, First Paragraph, Written Description Rejection

The Examiner rejected claims 20, 21, 24, and 29-31 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner interpreted claims 20, 21, 24 and 29, drawn to "an effective amount," to read on the genus

represented by an "amount effective to decrease or prevent in a subject the symptoms associated with a condition herein" (see p. 6, Office Action mailed 29 January 2003). The Examiner asserted that the specification does not reasonably convey that the Applicant was in possession of the genus of compounds represented by an "amount effective to decrease or prevent in a subject the symptoms associated with a condition herein." This rejection is respectfully traversed. However, to further prosecution, as recommended by the Examiner, the recitation "effective amount" has been removed from amended claims 20, 21, 24 and 29. Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

The 35 U.S.C. §112, First Paragraph, Enablement Rejection

The Examiner rejected claims 20, 21, 24, and 29-31 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner asserted that it would require undue experimentation of one of skill in the art to identify "an effective amount" of the compound as recited in the methods of claims 20, 21, 24 and 29. This rejection is respectfully traversed. However, to further prosecution, as recommended by the Examiner, the recitation "effective amount" has been removed from amended claims 20, 21, 24 and 29. Applicants respectfully request the withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claims 20, 21, 24, and 29-31 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed.

Specifically, the Examiner asserted that the recitation "the compound" in claim 29 lacks proper antecedent basis. Claim 29 has been amended to recite proper antecedent basis.

Further, the Examiner asserted that the metes and bounds of the recitation "an effective amount" in claims 20, 21, 24 and 29 are indefinite. In view of amendments to the claims to remove this recitation, withdrawal of this rejection is respectfully requested

For the reasons discussed above, withdrawal of the rejection of claims 20, 21, 24, and 29-31 under 35 U.S.C. §112, second paragraph, is respectfully requested.

The 35 U.S.C. §102 Rejection

The Examiner rejected claims 20, 21, and 29 under 35 U.S.C. § 102 as being anticipated by Rao et al. (*Neuron*, 19(801-812)1997). The Examiner asserted that Rao et al. discloses an assay that is the same as that claimed. Specifically, the Examiner asserted that Rao et al. discloses an assay that comprises contacting a cell with a compound (the compound APV) that alters the subcellular distribution NR1, activating an NMDA receptor (by administering NMDA itself), and detecting the distribution of NR1 in the cell that is the same as the assay of claims 20, 21, and 29.

This rejection is respectfully traversed. According to MPEP § 2131 a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."

The Examiner asserted that Rao et al. discloses contacting cells with both the compound APV and an activator of an NMDA receptor (NMDA itself) (see p.7 of the Office action mailed January 29, 2003). Applicants do not find any such disclosure of contacting cells with both APV and NMDA within the teachings of Rao et al. Examiner is invited to point out the exact portion of Rao et al. that provides such a teaching, of contacting of cells with both APV and NMDA.

Claim 20 and 29 are drawn to methods comprising the following three steps: 1) contacting a cell with a compound; 2) activating an NMDA glutamate receptor present on the cell; and 3) detecting the distribution of NR1 subunit in the cell, wherein the distribution of NR1

subunit in the cell contacted with the compound is altered relative to the distribution of NR1 subunit in a cell not contacted with the compound.

Rao et al. discloses contacting cells with three different compounds APV, TTX, and CNQX, all of which result in a shift in the distribution of NR1 to synaptic and spiny clusters (see p. 802, col. 1 and 2 and p. 804, col.1). However, in cells contacted with either APV or CNQX, the NMDA glutamate receptor present on the cells is never activated. And, more importantly, Rao et al. discloses that contacting cells with the TTX compound followed by activating the NMDA glutamate receptor (with NMDA itself) "largely *blocked* the increase in NR1 cluster number and a shift to synaptic sites induced by TTX" (see p. 804, col.1)(emphasis added). Thus, Rao et al. does not disclose a method that comprises all three steps of the methods of claims 20 and 29; contacting a cell with a compound, activating an NMDA glutamate receptor present on the cell, and detecting the distribution of NR1 subunit in the cell, wherein the distribution of NR1 subunit in the cell contacted with the compound is altered.

Claim 21 is drawn to a method for identifying compounds that alter the *amount* of NR1 subunit in a cell by contacting a cell with a compound; activating an NMDA glutamate receptor present on the cell; and detecting the *amount* of NR1 subunit in the cell; wherein an alteration in the *amount* of NR1 subunit in the cell contacted with the compound indicates the compound alters the *amount* of NR1 subunit. It is respectfully submitted that Rao et al. does not disclose an alteration in the *amount* of NR1 with the administration of a compound. Specifically, Rao et al. states that the effect of APV is due "solely to an increase in the number of NR1 clusters at synaptic sites . . . . that there is not a generalized increase in the amount of NR1 at all sites but indeed a shift in the distribution," and that the observed changes likely involve "relocation of previously existing receptor molecules" (see p. 802, col.2). Thus, Applicants respectfully submit that Rao et al does not disclose an increase in the amount of NR1 and can not anticipate claim 21.

Since the disclosure of Rao et al. does not set forth each and every element of claims 20, 21 and 29, Rao et al. can not anticipate claims 20, 21 and 29. Withdrawal of this rejection under 35 U.S.C. §102(b) is respectfully requested.

Summary

It is respectfully submitted that the pending claims 20, 21, 24, and 29-67 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

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PATENT TRADEMARK OFFICE

April 29, 2003
Date

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CERTIFICATE UNDER 37 CFR §1.10:
"Express Mail" mailing label number: EV073735039 US Date of Deposit: April 29, 2003
The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

By: _____
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APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 09/877,220
Docket No.: 265.00190101

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted.

In the Claims

For convenience, all pending claims are shown below.

20. [AMENDED] A method for identifying a compound that alters NR1 subunit distribution in a cell, the method comprising:

contacting a cell with [an effective amount of the] a compound;

activating an NMDA glutamate receptor present on the cell; and

detecting the distribution of NR1 subunit in the cell, wherein [detection of] an alteration in the distribution of NR1 subunit in the cell contacted with the compound relative to the distribution of NR1 subunit in a cell not contacted with the compound indicates [an alteration in] the compound alters the distribution of NR1 subunit in the cell.

21. [AMENDED] A method for identifying a compound that alters the amount of NR1 subunit [distribution] in a cell, the method comprising:

contacting a cell with [an effective amount of the] a compound;

activating an NMDA glutamate receptor present on the cell; and

detecting the [distribution] amount of NR1 subunit in the cell;

wherein [detection of] an alteration in the [distribution] amount of NR1 subunit in the cell contacted with the compound relative to the [distribution] amount of NR1 subunit in a cell not contacted with the compound indicates [an alteration in] the compound alters the amount [distribution] of NR1 subunit [, wherein] in the cell [is a neuron].

24. [AMENDED] A method for identifying a tyrosine kinase inhibitor that alters NR1 subunit distribution in a cell, the method comprising:

contacting a cell with [an effective amount of the] a tyrosine kinase inhibitor;

activating an NMDA glutamate receptor present in the cell; and

detecting the distribution of NR1 subunit in the cell, wherein [detection of] an alteration in the distribution of NR1 subunit in the cell contacted with the tyrosine kinase inhibitor relative to the distribution of NR1 subunit in a cell not contacted with the tyrosine kinase inhibitor indicates [an alteration in] the compound alters distribution of NR1 subunit.

29. [AMENDED] A method for altering NR1 subunit distribution in a cell, the method comprising:

contacting a cell with [an effective amount of the] a compound; [and]

activating an NMDA glutamate receptor present on the cell; and

detecting the distribution of NR1 subunit in the cell, wherein [detection of an alteration in] the distribution of NR1 subunit in the cell contacted with the compound is altered relative to the distribution of NR1 subunit in a cell not contacted with the compound [indicates an alteration in the distribution of NR1 subunit].

30. [AMENDED] The method of claim 29 wherein the amount of NR1 subunit associated with a nucleus of a cell [of the subject] contacted with a compound is decreased.

31. [AMENDED] The method of claim 29 wherein the amount of NR1 subunit associated with a nucleus of a cell [of the subject] is increased.

32. [NEW] The method of claim 20, wherein the cell is neuron.

33. [NEW] The method of claim 20, wherein the contacting a cell with a compound occurs before, during, or after activating an NMDA glutamate receptor present in the cell.

34. [NEW] The method of claim 20, wherein the alteration in the distribution of NR1 subunit in the cell is a decrease in the amount of NR1 subunit associated with the nucleus.

35. [NEW] The method of claim 20 wherein the alteration in the distribution of NR1 subunit in the cell is an increase in the amount of NR1 subunit associated with the nucleus.

36. [NEW] The method of claim 20, wherein the alteration in the distribution of NR1 subunit in the cell is a decrease in the total amount of NR1 subunit in the cell.

37. [NEW] The method of claim 20, wherein the alteration in the distribution of NR1 subunit in the cell is an increase in the total amount of NR1 subunit in the cell.

38. [NEW] The method of claim 20, wherein the compound is selected from the group consisting of a tyrosine kinase inhibitor, a tyrosine phosphatase and a serine/threonine phosphatase.

39. [NEW] The method of claim 20, wherein the compound is selected from the group consisting of a tyrosine kinase, a tyrosine phosphatase inhibitor, and a serine/threonine phosphatase inhibitor.

40. [NEW] The method of claim 20, wherein the alteration in the distribution of NR1 subunit in the cell is associated with a decrease in the amount of phosphorylated NR1 subunit in the cell.

41. [NEW] The method of claim 20, wherein the alteration in the distribution of NR1 subunit in the cell is associated with an increase in the amount of phosphorylated NR1 subunit in the cell.

42. [NEW] The method of claim 21, wherein the cell is neuron.

43. [NEW] The method of claim 21, wherein the contacting a cell with a compound occurs before, during, or after activating an NMDA glutamate receptor present in the cell.

44. [NEW] The method of claim 21, wherein the alteration in the amount of NR1 subunit in the cell is a decrease in the total amount of NR1 subunit in the cell.

45. [NEW] The method of claim 21, wherein the alteration in the amount of NR1 subunit in the cell is an increase in the total amount of NR1 subunit in the cell.

46. [NEW] The method of claim 21, wherein the alteration in the amount of NR1 subunit in the cell is a decrease in the amount of NR1 subunit associated with the nucleus.

47. [NEW] The method of claim 21, wherein the alteration in the amount of NR1 subunit in the cell is an increase in the amount of NR1 subunit associated with the nucleus.

48. [NEW] The method of claim 21, wherein the compound is selected from the group consisting of a tyrosine kinase inhibitor, a tyrosine phosphatase and a serine/threonine phosphatase.

49. [NEW] The method of claim 21, wherein the compound is selected from the group consisting of a tyrosine kinase, a tyrosine phosphatase inhibitor, and a serine/threonine phosphatase inhibitor.

50. [NEW] The method of claim 21, wherein the alteration in the distribution of NR1 subunit in the cell is associated with a decrease in the amount of phosphorylated NR1 subunit in the cell.

51. [NEW] The method of claim 21, wherein the alteration in the distribution of NR1 subunit in the cell is associated with an increase in the amount of phosphorylated NR1 subunit in the cell.

52. [NEW] The method of claim 24 wherein the cell is a neuron.

53. [NEW] The method of claim 24, wherein the contacting a cell with a tyrosine kinase inhibitor occurs before, during, or after activating an NMDA glutamate receptor present in the cell.

54. [NEW] The method of claim 24, wherein the alteration in the distribution of NR1 subunit in the cell is a decrease in the amount of NR1 subunit associated with the nucleus.

55. [NEW] The method of claim 24, wherein the alteration in the distribution of NR1 subunit in the cell is an increase in the amount of NR1 subunit associated with the nucleus.

56. [NEW] The method of claim 24, wherein the alteration in the distribution of NR1 subunit in the cell is a decrease in the total amount of NR1 subunit in the cell.

57. [NEW] The method of claim 24, wherein the alteration in the distribution of NR1 subunit in the cell is an increase in the total amount of NR1 subunit in the cell.

58. [NEW] The method of claim 24, wherein the alteration in the distribution of NR1 subunit in the cell is associated with a decrease in the amount of phosphorylated NR1 subunit in the cell.

59. [NEW] The method of claim 24, wherein the alteration in the distribution of NR1 subunit in the cell is associated with an increase in the amount of phosphorylated NR1 subunit in the cell.

60. [NEW] The method of claim 29 wherein the cell is a neuron.

61. [NEW] The method of claim 29, wherein the contacting a cell with a compound occurs before, during, or after activating a NMDA glutamate receptor present in the cell.

62. [NEW] The method of claim 29, wherein the total amount of NR1 subunit in the cell is decreased.

63. [NEW] The method of claim 29, wherein the total amount of NR1 subunit in the cell is increased.

64. [NEW] The method of claim 29, wherein the amount of phosphorylated NR1 subunit in the cell is decreased.

65. [NEW] The method of claim 29, wherein the amount of phosphorylated NR1 subunit in the cell is increased.

66. [NEW] The method of claim 29, wherein the compound is selected from the group consisting of a tyrosine kinase inhibitor, a tyrosine phosphatase and a serine/threonine phosphatase.

67. [NEW] The method of claim 29, wherein the compound is selected from the group consisting of a tyrosine kinase, a tyrosine phosphatase inhibitor, and a serine/threonine phosphatase inhibitor.